

Supporting Information

False Positives in a Reporter Gene Assay: Identification and Synthesis of Substituted N-Pyridin-2-yl-benzamides as Competitive Inhibitors of Firefly Luciferase.

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Experimental and spectroscopic data

N-Quinolin-2-yl-benzamide (1).¹ Starting from 2-amino-quinoline. Yield 31%; white solid, recrystallized from ethanol. ¹H-NMR δ (CDCl₃): 8.99 (br s, 1H, NH), 8.59 (d, 1H, J = 9.1 Hz, quinoline-H), 8.21 (d, 1H, J = 8.8 Hz, quinoline-H), 8.01-7.96 (m, 2H, phenyl-H), 7.84-7.77 (m, 2H, quinoline-H), 7.66 (dd, 1H, J¹ = 8.4 Hz, J² = 1.5 Hz, quinoline-H), 7.56-7.41 (m, 4H, phenyl-H + quinoline-H). ¹³C-NMR δ (CDCl₃): 151.1, 146.5, 141.0, 138.5, 134.1, 132.3, 129.9, 129.2, 128.7, 127.5, 127.2, 125.1, 114.3, 114.1.

General procedure for the preparation of 2a and 13-21.² Under a nitrogen atmosphere 2-amino-5-bromo-pyridine (1.0 equiv), the appropriate substituted boronic acid (1.3 equiv) and Na₂CO₃ (2.6 equiv) were dissolved in a mixture of water and DMF (1:4), followed by the addition of Pd(OAc)₂ (0.01 equiv). The reaction mixture was heated at 110 °C for 3 hours. After cooling to room temperature, it was diluted with water and the organic materials extracted with ethyl acetate. The organic layer was washed with water and brine, dried over MgSO₄ and concentrated *in vacuo*. The crude products were purified by silica column chromatography, eluting with ethyl acetate or with a 0-3% methanol in dichloromethane mixture. The solid products were obtained in a 26-65% yield.

2-Amino-5-phenylpyridine (2a).² Yield 34%; white solid. ¹H-NMR δ (CDCl₃): 8.32 (d, 1H, J = 2.5 Hz, pyridine-H), 7.68 (dd, 1H, J¹ = 8.4 Hz, J² = 2.5 Hz, pyridine-H), 7.52-7.31 (m, 5H, phenyl-H), 6.58 (d, 1H, J = 8.4 Hz, pyridine-H), 4.51 (br s, 1H, NH₂).

5-(4-Chloro-phenyl)-pyridin-2ylamine (13). Yield 26%; off white solid. ¹H-NMR δ (CDCl₃): 8.28 (d, 1H, J = 2.2 Hz, pyridine-H), 7.63 (dd, 1H, J¹ = 8.6 Hz, J² = 2.2 Hz, pyridine-H), 7.45-7.35 (m, 4H, Ar-H), 6.57 (d, 1H, J = 8.4 Hz, pyridine-H), 4.55 (br s, 1H, NH₂).

5-(4-Methoxy-phenyl)-pyridin-2ylamine (14). Yield 64%; white solid. ¹H-NMR δ (CDCl₃): 8.28 (d, 1H, J = 2.5 Hz, pyridine-H), 7.62 (dd, 1H, J¹ = 8.6 Hz, J² = 2.6 Hz, pyridine-H), 7.42 (d, 2H, J = 8.8 Hz, Ar-H), 6.97 (d, 2H, J = 8.4 Hz, Ar-H), 6.56 (d, 1H, J = 8.4 Hz, pyridine-H), 4.50 (br s, 1H, NH₂), 3.84 (s, 3H, OCH₃).

5-(4-Methyl-phenyl)-pyridin-2ylamine (15). Yield 59%; white solid. ¹H-NMR δ (CDCl₃): 8.34 (d, 1H, J = 2.6 Hz, pyridine-H), 7.65 (dd, 1H, J¹ = 8.4 Hz, J² = 2.6 Hz, pyridine-H), 7.39 (d, 2H, J = 8.1 Hz, Ar-H), 7.23 (d, 2H, J = 8.4 Hz, Ar-H), 6.56 (d, 1H, J = 8.4 Hz, pyridine-H), 4.58 (br s, 1H, NH₂), 2.38 (s, 3H, CH₃).

5-(3-Chloro-phenyl)-pyridin-2ylamine (16). Yield 62%; white solid. ¹H-NMR δ (CDCl₃): 8.29 (d, 1H, J = 2.6 Hz, pyridine-H), 7.63 (dd, 1H, J¹ = 8.7 Hz, J² = 2.6 Hz, pyridine-H), 7.47 (s, 1H, Ar-H), 7.39-7.24 (m, 3H, Ar-H), 6.57 (d, 1H, J = 8.4 Hz, pyridine-H), 4.58 (br s, 1H, NH₂).

5-(4-Dimethylamino-phenyl)-pyridin-2ylamine (17). Yield 52%; yellowish solid. ¹H-NMR δ (CDCl₃): 8.28 (s, 1H, pyridine-H), 7.62 (d, 1H, J = 8.4 Hz, pyridine-H), 7.39 (d, 2H, J = 8.7 Hz, Ar-H), 7.79 (d, 2H, J = 9.1 Hz, Ar-H), 6.55 (d, 1H, J = 8.4 Hz, pyridine-H), 4.42 (br s, 1H, NH₂), 2.95 (s, 6H, N(CH₃)₂).

5-(4-Isopropoxy-phenyl)-pyridin-2ylamine (18). Yield 65%; white solid. ¹H-NMR δ (CDCl₃): 8.30 (d, 1H, J = 2.6 Hz, pyridine-H), 7.61 (dd, 1H, J¹ = 8.6 Hz, J² = 2.6 Hz, pyridine-H), 7.40 (d, 2H, J = 8.4 Hz, Ar-H), 6.93 (d, 2H, J = 8.4 Hz, Ar-H), 6.55 (d, 1H, J = 8.4 Hz, pyridine-H), 4.60-4.51 (m, 3H, CH(CH₃)₂ + NH₂), 1.37 (s, 3H, CH(CH₃)₂), 1.34 (s, 3H, CH(CH₃)₂).

5-(4-*tert*-Butyl-phenyl)-pyridin-2-ylamine (19). Yield 46%; white solid. ¹H-NMR δ (CDCl₃): 8.35 (d, 1H, J = 2.2 Hz, pyridine-*H*), 7.67 (dd, 1H, J¹ = 8.5 Hz, J² = 2.4 Hz, pyridine-*H*), 7.45 (m, 4H, Ar-*H*), 6.55 (d, 1H, J = 8.4 Hz, pyridine-*H*), 4.55 (s br, 2H, NH₂), 1.35 (s, 6H, C(CH₃)₃).

5-(4-Trifluoromethyl-phenyl)-pyridin-2-ylamine (20). Yield 45%; white solid. ¹H-NMR δ (CDCl₃): 8.36 (d, 1H, J = 2.2 Hz, pyridine-*H*), 7.71-7.57 (m, 5H, pyridine-*H* + Ar-*H*), 6.60 (d, 1H, J = 8.8 Hz, pyridine-*H*), 4.73 (br s, 1H, NH₂).

5-(3,4-Dichloro-phenyl)-pyridin-2-ylamine (21). Yield 62%; white solid. ¹H-NMR δ (CDCl₃): 8.30 (d, 1H, J = 2.6 Hz, pyridine-*H*), 7.65-7.56 (m, 2H, Ar-*H* + pyridine-*H*), 7.47 (d, 1H, J = 8.4 Hz, Ar-*H*), 7.30 (dd, 1H, J¹ = 8.3 Hz, J² = 2.2 Hz, Ar-*H*), 6.58 (d, 1H, J = 8.4 Hz, pyridine-*H*), 4.72 (br s, 2H, NH₂).

General procedure for the preparation of 3-7, 9, 11, 12 and 22-39.³ The appropriate acid chloride (1.1 mmol) was added to a solution of 2-amino-5-phenylpyridine (1.0 mmol) in pyridine (4 mL) at room temperature under a nitrogen atmosphere. According to TLC the reaction went to completion after 2 hours. The organic material was extracted with DCM, dried over MgSO₄ and evaporated under reduced pressure. The crude product was purified by column chromatography, eluting with a mixture of 0.5-2% methanol and chloroform or 0.5-2% methanol and dichloromethane resulting in a yield of 31-75% of the desired products.

2,4-Dimethoxy-N-(5-methyl-pyridin-2-yl)benzamide (3). Starting from 2-amino-5-methylpyridine. Yield 54%; white solid. ¹H-NMR δ (CDCl₃): 10.17 (br s, 1H, NH), 8.31 (d, 1H, J = 8.4 Hz, pyridine-*H*), 8.24 (d, 1H, J = 9.1 Hz, Ar-*H*), 8.13 (s, 1H, pyridine-*H*), 7.52 (d, 1H, J = 8.4 Hz, pyridine-*H*), 6.63 (dd, 1H, J¹ = 8.8 Hz, J² = 2.2 Hz, Ar-*H*), 6.53 (d, 1H, J = 2.2 Hz, Ar-*H*), 4.04 (s, 3H, OCH₃), 3.86 (s, 3H, OCH₃), 2.29 (s, 3H, CH₃). ¹³C-NMR δ (CDCl₃): 163.7, 162.9, 158.6, 149.7, 147.5, 138.4, 133.8, 128.3, 114.0, 113.8, 105.0, 98.2, 55.9, 55.2, 17.5.

N-Pyridin-2-ylbenzamide (4). Starting from 2-amino-pyridine. Yield 69%; white solid. ¹H-NMR δ (DMSO): 10.81 (br s, 1H, NH), 8.41 (d, 1H, J = 2.9 Hz, pyridine-*H*), 8.22 (d, 1H, J = 8.0, pyridine-*H*), 8.07-8.03 (m, 2H, phenyl-*H*), 7.87 (dd, 1H, J¹ = 7.3 Hz, J² = 1.5 Hz, pyridine-*H*), 7.66-7.49 (m, 3H, phenyl-*H*), 7.19 (dd, 1H, J¹ = 6.2 Hz, J² = 2.2 Hz, pyridine-*H*). ¹³C-NMR δ (CDCl₃): 165.7, 151.4, 147.6, 138.2, 134.1, 132.0, 128.5, 127.1, 119.7, 114.0.

N-(6-Phenylpyridin-2-yl)benzamide (5). Starting from 2-amino-6-phenylpyridine. Yield 64%; white solid. ¹H-NMR δ (DMSO): 10.76 (br s, 1H, NH), 8.25-8.06 (m, 5H, phenyl-*H* + pyridine-*H*), 7.98-7.73 (m, 2H, pyridine-*H*), 7.60-7.43 (m, 6H, phenyl-*H*). ¹³C-NMR δ (CDCl₃): 165.7, 155.9, 151.2, 139.1, 138.6, 134.2, 132.1, 129.0, 128.7, 128.6, 127.1, 126.7, 116.6, 112.3.

N-(5-Phenylpyridin-2-yl)benzamide (6). Yield 46%; white solid. ¹H-NMR δ (CDCl₃): 8.83 (br s, 1H, NH), 8.50-8.46 (m, 2H, pyridine-*H*), 8.00-7.93 (m, 3H, pyridine-*H* + phenyl-*H*), 7.58-7.38 (m, 8H, phenyl-*H*). ¹³C-NMR δ (CDCl₃): 166.3, 150.9, 145.7, 137.0, 136.6, 134.5, 132.5, 131.9, 128.8, 128.5, 127.6, 127.4, 126.4, 114.1.

N-(5-Methylpyridin-2-yl)benzamide (7). Starting from 2-amino-5-methylpyridine.⁴ Yield 49%; white solid. ¹H-NMR δ (CDCl₃): 8.93 (br s, 1H, NH), 8.29 (d, 1H, J = 8.4 Hz, pyridine-*H*), 7.98-7.89 (m, 3H, phenyl-*H* + pyridine-*H*), 7.58-7.43 (m, 4H, phenyl-*H* + pyridine-*H*), 2.28 (s, 3H, CH₃). ¹³C-NMR δ (CDCl₃): 166.2, 149.7, 147.3, 138.6, 134.6, 131.4, 128.6, 128.2, 127.3, 113.8, 17.4.

Phenyl N-(5-phenylpyridin-2-yl)carbamate (9). Starting from phenyl chloroformate. Yield 47%; white solid. ¹H-NMR δ (CDCl₃): 9.60 (br s, 1H, NH), 8.67

(d, 1H, $J = 2.6$ Hz, pyridine-*H*), 8.13 (d, 1H, $J = 8.4$ Hz, pyridine-*H*), 7.96 (dd, 1H, $J^1 = 8.7$ Hz, $J^2 = 2.2$ Hz, pyridine-*H*), 7.56-7.23 (m, 10H, phenyl-*H*). $^{13}\text{C-NMR}$ δ (CDCl_3): 151.5, 150.6, 150.2, 145.8, 136.9, 132.1, 129.3, 128.8, 127.5, 126.4, 125.7, 121.4, 112.3.

N-(5-Phenylpyridin-2-yl)butanamide (11). Yield 66%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.49 (br s, 1H, *NH*), 8.33-8.29 (m, 2H, pyridine-*H*), 7.92 (dd, 1H, $J^1 = 8.8$ Hz, $J^2 = 2.2$ Hz, pyridine-*H*), 7.57-7.37 (m, 5H, phenyl-*H*), 2.40 (t, 2H, $J = 7.66$ Hz, $\text{COCH}_2\text{CH}_2\text{CH}_3$), 1.84-1.73 (m, 2H, $\text{COCH}_2\text{CH}_2\text{CH}_3$), 1.02 (t, 3H, $J = 7.3$ Hz, $\text{COCH}_2\text{CH}_2\text{CH}_3$). $^{13}\text{C-NMR}$ δ (DMSO): 172.2, 151.5, 145.7, 136.9, 136.1, 131.0, 129.1, 127.6, 126.3, 113.4, 38.1, 18.5, 13.6.

N-(5-Phenylpyridin-2-yl)cyclohexanecarboxamide (12). Yield 69%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.49 (d, 1H, $J = 2.2$ Hz, pyridine-*H*), 8.31 (d, 1H, $J = 8.4$ Hz, pyridine-*H*), 8.16 (br s, 1H, *NH*), 7.91 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.5$ Hz, pyridine-*H*), 7.58-7.37 (m, 5H, phenyl-*H*), 2.36-2.22 (m, 1H, $J = 7.66$ Hz, *CH*-cyclohexane), 2.02-1.25 (m, 10H, *CH*₂-cyclohexane). $^{13}\text{C-NMR}$ δ (CDCl_3): 174.9, 150.9, 145.4, 136.9, 137.2, 136.7, 132.4, 128.8, 127.5, 126.4, 114.0, 46.1, 29.3, 25.4.

N-[5-(4-Chlorophenyl)pyridin-2-yl]benzamide (22). Yield 53%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.86 (br s, 1H, *NH*), 8.48 (d, 1H, $J = 8.76$ Hz, pyridine-*H*), 8.43 (d, 1H, $J = 2.6$ Hz, pyridine-*H*), 7.97-7.91 (m, 3H, pyridine-*H* + phenyl-*H*), 7.59-7.40 (m, 7H, phenyl-*H* + Ar-*H*). $^{13}\text{C-NMR}$ δ (CDCl_3): 165.8, 150.9, 145.6, 136.5, 135.5, 134.2, 133.8, 132.0, 131.4, 129.0, 128.6, 127.7, 127.2, 113.9.

N-[5-(4-Methoxyphenyl)pyridin-2-yl]benzamide (23). Yield 68%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.80 (br s, 1H, *NH*), 8.47-8.43 (m, 2H, pyridine-*H*), 7.97-7.90 (m, 3H, pyridine-*H* + phenyl-*H*), 7.62-7.48 (m, 5H, phenyl-*H* + Ar-*H*), 7.00 (d, 2H, $J = 8.7$ Hz, Ar-*H*), 3.86 (s, 3H, OCH_3). $^{13}\text{C-NMR}$ δ (CDCl_3): 165.8, 159.3, 150.2, 145.3, 136.1, 134.3, 132.4, 131.9, 129.5, 128.5, 127.5, 127.2, 114.3, 113.9, 55.1.

N-[5-(4-Methylphenyl)pyridin-2-yl]benzamide (24). Yield 41%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.89 (br s, 1H, *NH*), 8.46-8.45 (m, 2H, pyridine-*H*), 7.97-7.94 (m, 3H, pyridine-*H* + phenyl-*H*), 7.59-7.56 (m, 1H, phenyl-*H*), 7.52-7.49 (m, 2H, phenyl-*H*), 7.46 (d, 2H, $J = 8.0$ Hz, Ar-*H*), 7.28 (d, 2H, $J = 8.0$ Hz, Ar-*H*), 2.28 (s, 3H, CH_3). $^{13}\text{C-NMR}$ δ (CDCl_3): 165.8, 150.5, 145.8, 137.7, 136.6, 134.4, 134.3, 133.0, 132.2, 129.7, 128.7, 127.3, 126.6, 114.0, 21.1.

N-[5-(3-Chlorophenyl)pyridin-2-yl]benzamide (25). Yield 43%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 9.07 (br s, 1H, *NH*), 8.50 (d, 1H, $J = 8.8$ Hz, pyridine-*H*), 8.35 (d, 1H, $J = 2.6$ Hz, pyridine-*H*), 7.96-7.91 (m, 3H, pyridine-*H* + phenyl-*H*), 7.63-7.32 (m, 7H, Ar-*H* + phenyl-*H*). $^{13}\text{C-NMR}$ δ (CDCl_3): 166.2, 151.3, 145.7, 138.8, 136.6, 134.7, 134.4, 132.1, 131.1, 130.0, 128.6, 127.5, 127.3, 126.4, 124.5, 113.9.

N-[5-(4-Dimethylamino-phenyl)pyridin-2-yl]benzamide (26). Yield 75%; off-white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.86 (br s, 1H, *NH*), 8.43 (s, 1H, pyridine-*H*), 8.41 (d, 1H, $J = 4.7$ Hz, pyridine-*H*), 7.97-7.89 (m, 3H, pyridine-*H* + phenyl-*H*), 7.57-7.43 (m, 5H, Ar-*H* + phenyl-*H*), 5.85 (s, 6H, $\text{N}(\text{CH}_3)_2$). $^{13}\text{C-NMR}$ δ (CDCl_3): 165.6, 150.0, 149.5, 144.7, 135.7, 134.3, 132.9, 131.8, 128.5, 127.1, 124.8, 113.9, 112.6, 40.2.

N-[5-(4-Isopropoxy-phenyl)pyridin-2-yl]benzamide (27). Yield 65%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.87 (br s, 1H, *NH*), 8.46-8.42 (m, 2H, pyridine-*H*), 7.97-8.89 (m, 3H, phenyl-*H* + pyridine-*H*), 7.58-7.43 (m, 5H, Ar-*H* + phenyl-*H*), 6.98 (d, 2H, $J = 9.1$ Hz, Ar-*H*), 4.60 (q, 1H, $J = 6.2$ Hz, $\text{OCH}(\text{CH}_3)_2$), 1.39 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). $^{13}\text{C-NMR}$ δ (CDCl_3): 166.2, 156.6, 150.4, 145.2, 135.9, 134.6, 132.2, 131.8, 129.1, 128.4, 127.5, 116.0, 114.2, 69.7, 21.8.

N-[5-(4-tert-Butylphenyl)pyridin-2-yl]benzamide (28). Yield 34%; white solid. $^1\text{H-NMR}$ δ (CDCl_3): 8.98 (br s, 1H, *NH*), 8.49-8.43 (m, 2H, pyridine-*H*), 7.99-7.92

(m, 3H, pyridine-*H* + phenyl-*H*), 7.57-7.45 (m, 7H, Ar-*H* + phenyl-*H*), 1.37 (s, 9H, *t*-butyl). $^{13}\text{C-NMR } \delta$ (CDCl_3): 166.1, 150.7, 145.6, 136.5, 134.4, 134.1, 132.4, 131.9, 128.5, 127.3, 126.1, 125.8, 114.1, 34.4, 31.1.

N-{5-[4-(Trifluoromethyl)phenyl]pyridin-2-yl}benzamide (29). Yield 52%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 9.11 (br s, 1H, *NH*), 8.52 (d, 1H, $J = 8.4$ Hz, pyridine-*H*), 8.40 (d, 1H, $J = 2.2$ Hz, pyridine-*H*), 8.00-7.93 (m, 3H, pyridine-*H* + phenyl-*H*), 7.73-7.47 (m, 7H, Ar-*H* + phenyl-*H*). $^{13}\text{C-NMR } \delta$ (CDCl_3): 165.9, 151.4, 145.9, 140.6, 136.7, 134.1, 132.1, 131.1, 128.6, 127.2, 126.7, 125.7, 116.0, 113.9.

N-[5-(3,4-Dichlorophenyl)pyridin-2-yl]benzamide (30). Yield 49%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.74 (br s, 1H, *NH*), 8.51-8.45 (m, 2H, pyridine-*H*), 7.96-7.90 (m, 3H, pyridine-*H* + phenyl-*H*), 7.65-7.37 (m, 6H, Ar-*H* + phenyl-*H*). $^{13}\text{C-NMR } \delta$ (DMSO): 166.2, 152.2, 146.1, 137.5, 136.4, 134.0, 132.1, 132.0, 131.1, 130.5, 129.0, 128.4, 128.2, 128.1, 126.6, 114.4.

4-Chloro-N-(5-phenylpyridin-2-yl)benzamide (31). Yield 41%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.85 (br s, 1H, *NH*), 8.47-8.43 (m, 2H, pyridine-*H*), 7.98 (d, 1H, $J = 8.0$ Hz, pyridine-*H*), 7.90 (dd, 2H, $J^1 = 8.8$ Hz, $J^2 = 1.5$ Hz, Ar-*H*), 7.58-7.35 (m, 7H, Ar-*H* + phenyl-*H*). $^{13}\text{C-NMR } \delta$ (DMSO): 165.1, 151.4, 146.2, 136.9, 136.8, 136.3, 132.9, 131.7, 130.1, 129.2, 128.5, 127.9, 126.5, 114.6, 126.6.

4-Methoxy-N-(5-phenylpyridin-2-yl)benzamide (32). Yield 69%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.93 (br s, 1H, *NH*), 8.49-8.41 (m, 2H, pyridine-*H*), 7.99-7.90 (m, 3H, pyridine-*H* + Ar-*H*), 7.56-7.37 (m, 5H, phenyl-*H*), 6.98 (d, 2H, $J = 8.8$ Hz, Ar-*H*), 3.90 (s, 3H, OCH_3). $^{13}\text{C-NMR } \delta$ (CDCl_3): 165.8, 162.5, 151.2, 145.7, 137.0, 136.5, 132.1, 129.4, 128.8, 127.5, 126.7, 126.4, 114.0, 113.7, 55.2.

4-Methyl-N-(5-phenylpyridin-2-yl)benzamide (33). Yield 70%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.96 (br s, 1H, *NH*), 8.47 (dd, 1H, $J^1 = 8.8$ Hz, $J^2 = 0.8$ Hz, pyridine-*H*), 8.41 (d, 1H, $J = 2.2$ Hz, pyridine-*H*), 7.96 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.6$ Hz, pyridine-*H*), 7.84 (d, 2H, $J = 8.0$ Hz, Ar-*H*), 7.57-7.27 (m, 7H, Ar-*H* + phenyl-*H*), 2.41 (s, 3H, CH_3). $^{13}\text{C-NMR } \delta$ (CDCl_3): 166.2, 151.0, 145.8, 142.5, 137.1, 136.5, 132.3, 131.7, 129.1, 128.8, 127.4, 127.3, 126.4, 113.9, 21.2.

3-Chloro-N-(5-phenylpyridin-2-yl)benzamide (34). Yield 59%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.74 (br s, 1H, *NH*), 8.51 (dd, 1H, $J^1 = 2.2$ Hz, $J^2 = 0.7$ Hz, pyridine-*H*), 8.44 (dd, 1H, $J^1 = 8.4$ Hz, $J^2 = 0.7$ Hz, pyridine-*H*), 8.01 (d, 1H, $J = 2.6$ Hz, pyridine-*H*), 7.96 (dd, 1H, $J^1 = 3.5$ Hz, $J^2 = 1.8$ Hz, Ar-*H*), 7.83-7.78 (m, 1H, Ar-*H*), 7.60-7.35 (m, 7H, Ar-*H* + phenyl-*H*). $^{13}\text{C-NMR } \delta$ (DMSO): 164.7, 151.4, 145.8, 136.8, 133.3, 131.7, 130.3, 129.1, 128.0, 127.8, 126.8, 126.5, 114.7.

3,4-Dichloro-N-(5-phenylpyridin-2-yl)benzamide (35). Yield 45%; white solid. $^1\text{H-NMR } \delta$ (DMSO): 11.17 (br s, 1H, *NH*), 8.75 (s, 1H, pyridine-*H*), 8.32-8.17 (m, 3H, Ar-*H* + pyridine-*H*), 8.02 (d, 1H, $J = 8.8$ Hz, Ar-*H*), 7.83-7.74 (m, 3H, Ar-*H* + phenyl-*H*), 7.55-7.41 (m, 3H, phenyl-*H*). $^{13}\text{C-NMR } \delta$ (DMSO): 163.8, 151.2, 145.8, 136.7, 136.1, 134.8, 134.4, 131.8, 131.4, 130.6, 130.1, 129.1, 128.3, 127.8, 126.5, 114.6.

2,4-Dimethoxy-N-(5-phenylpyridin-2-yl)benzamide (36). Yield 44%; white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 10.32 (br s, 1H, *NH*), 8.55 (d, 1H, $J = 2.2$ Hz, pyridine-*H*), 8.50 (d, 1H, $J^1 = 8.8$ Hz, pyridine-*H*), 8.26 (d, 1H, $J = 8.8$ Hz, Ar-*H*), 7.93 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.6$ Hz, pyridine-*H*), 7.60-7.37 (m, 5H, phenyl-*H*), 6.65 (dd, 1H, $J^1 = 8.9$ Hz, $J^2 = 2.6$ Hz, Ar-*H*), 6.53 (d, 1H, $J = 2.2$ Hz, Ar-*H*), 4.06 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3). $^{13}\text{C-NMR } \delta$ (CDCl_3): 163.8, 163.0, 158.7, 151.2, 145.7, 137.3, 136.2, 133.8, 131.9, 128.8, 127.3, 126.4, 114.1, 113.9, 105.5, 98.2, 55.8, 55.2.

4-Amino-N-(5-phenylpyridin-2-yl)benzamide (37). Yield 33%; off-white solid. $^1\text{H-NMR } \delta$ (CDCl_3): 8.67 (br s, 1H, *NH*), 8.49-8.43 (m, 2H, pyridine-*H*), 7.95 (dd,

1H, $J^1 = 8.6$ Hz, $J^2 = 2.2$ Hz, pyridine-*H*), 7.78 (d, 2H, $J = 8.4$ Hz, Ar-*H*), 7.50-7.33 (m, 5H, phenyl-*H*), 6.70 (d, 2H, $J = 8.8$ Hz, Ar-*H*), 4.09 (br s, 2H, NH_2). ^{13}C -NMR δ (DMSO): 165.7, 152.6, 152.1, 145.5, 137.0, 136.0, 130.9, 129.9, 129.2, 127.7, 126.4, 120.2, 114.3, 112.7.

4-Isopropoxy-N-(5-phenylpyridin-2-yl)benzamide (38). Starting from 4-isopropoxy-benzoyl chloride.⁵ Yield 32%; white solid. 1H -NMR δ ($CDCl_3$): 8.86 (br s, 1H, *NH*), 8.48-8.44 (m, 2H, pyridine-*H*), 7.98-7.87 (m, 3H, Ar-*H* + pyridine-*H*), 7.57-7.37 (m, 5H, phenyl-*H*), 6.95 (d, 2H, $J = 8.8$ Hz, Ar-*H*), 4.72-4.54 (m, 1H, $OCH(CH_3)_2$), 1.38 (s, 3H, $OCH(CH_3)_2$), 1.34 (s, 3H, $OCH(CH_3)_2$). ^{13}C -NMR δ ($CDCl_3$): 165.8, 161.0, 151.3, 145.7, 137.1, 136.5, 132.1, 129.4, 128.8, 127.4, 126.4, 126.2, 115.1, 114.0, 69.8, 21.6.

4-Dimethylamino-N-(5-phenylpyridin-2-yl)benzamide (39). Starting from the *tert*-butyloxycarbonyl protected 4-amino-benzoyl chloride.^{6,7} Yield 52%; white solid. 1H -NMR δ ($CDCl_3$): 8.64 (br s, 1H, *NH*), 8.49-8.46 (m, 2H, pyridine-*H*), 7.95 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.2$ Hz, pyridine-*H*), 7.85 (d, 2H, $J = 9.1$ Hz, Ar-*H*), 7.60-7.37 (m, 5H, phenyl-*H*), 6.71 (d, 2H, $J = 9.1$ Hz, Ar-*H*), 3.05 (s, 6H, $N(CH_3)_2$). ^{13}C -NMR δ ($CDCl_3$): 165.9, 152.6, 151.5, 145.8, 137.3, 136.4, 131.8, 129.0, 128.8, 127.4, 126.4, 120.6, 113.7, 110.8, 39.7.

Procedure for the preparation of 8. A solution of 2-amino-5-phenyl-pyridine (300 mg, 1.76 mmol) and benzyl chloride (405 μ L, 3.52 mmol) in pyridine (3.5 mL) was heated in a closed vessel in the microwave at 180 °C for 2 hours. The reaction mixture was poured in water, adjusted to pH = 10 with 1 M NaOH and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and the solvents were evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using DCM/methanol (99/1), followed by recrystallization from methanol, yielding 78 mg (17% yield) of the crystalline product.

N-(5-Phenylpyridin-2-yl)benzylamine (8). Yield 17%; white solid. 1H -NMR δ ($CDCl_3$): 8.36 (d, 1H, $J = 2.6$ Hz, pyridine-*H*), 7.65 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.5$ Hz, pyridine-*H*), 7.52-7.27 (m, 10H, phenyl-*H*), 6.45 (d, 1H, $J = 8.8$ Hz, pyridine-*H*), 5.03 (br s, 1H, *NH*), 4.55 (d, 2H, $J = 5.9$ Hz, CH_2). ^{13}C -NMR δ ($CDCl_3$): 157.9, 146.3, 139.0, 138.3, 136.1, 128.7, 128.5, 127.3, 127.1, 126.5, 126.0, 106.4, 46.2.

Procedure for the preparation of 10. The 2-amino-5-phenylpyridine (250 mg, 1.47 mmol) was dissolved in dioxane (2 mL) and phenyl isocyanate (160 μ L, 1.47 mmol) was added at room temperature under a nitrogen atmosphere. After 4 hours the formed precipitate was collected by filtration and washed with chloroform with a yield of 84%.

1-Phenyl-3-(5-phenylpyridin-2-yl)urea (10). Yield 84%; white solid. 1H -NMR δ (DMSO): 10.41 (br s, 1H, *NH*), 9.55 (s, 1H, *NH*), 8.64 (d, 1H, $J = 1.8$ Hz, pyridine-*H*), 8.10 (dd, 1H, $J^1 = 8.6$ Hz, $J^2 = 2.5$ Hz, pyridine-*H*), 7.73-7.30 (m, 10H, phenyl-*H*), 7.08-7.01 (m, 1H, pyridine-*H*). ^{13}C -NMR δ (DMSO): 152.2, 144.8, 139.1, 136.9, 136.7, 129.5, 129.1, 127.6, 126.3, 122.6, 118.9, 111.9.

Elemental Analyses

Comp.	Mol. Formula	Theoretical (%)			Experimental (%)		
		C	H	N	C	H	N
1	C ₁₆ H ₁₂ N ₂ O*0.05EtOH	76.69	4.83	11.18	76.40	4.54	11.53
3	C ₁₅ H ₁₆ N ₂ O ₃	66.16	5.92	10.29	65.99	6.07	10.20
4	C ₁₂ H ₁₀ N ₂ O	72.71	5.08	14.13	72.49	5.22	13.91
5	C ₁₈ H ₁₄ N ₂ O	78.81	5.14	10.21	78.47	5.17	10.38
6	C ₁₈ H ₁₄ N ₂ O*0.04CHCl ₃	77.67	5.07	10.04	77.68	4.81	10.12
7	C ₁₃ H ₁₂ N ₂ O	73.57	5.70	13.20	73.17	5.87	13.34
8	C ₁₈ H ₁₆ N ₂	83.05	6.19	10.76	82.75	6.03	10.74
9	C ₁₈ H ₁₄ N ₂ O ₂ *0.05CHCl ₃	73.13	4.77	9.45	73.11	4.69	9.63
10	C ₁₈ H ₁₅ N ₃ O*0.12CHCl ₃	71.46	5.01	13.79	71.46	4.89	13.86
11	C ₁₅ H ₁₆ N ₂ O*0.02CHCl ₃	74.44	6.66	11.56	74.45	6.57	11.58
12	C ₁₈ H ₂₀ N ₂ O *0.02CHCl ₃	76.59	7.14	9.91	76.60	7.01	9.97
22	C ₁₈ H ₁₃ ClN ₂ O*0.04CHCl ₃	69.06	4.18	8.93	69.05	4.10	9.05
23	C ₁₉ H ₁₆ N ₂ O ₂ *0.06CHCl ₃	73.39	5.19	8.98	73.35	5.42	9.14
24	C ₁₉ H ₁₆ N ₂ O	79.14	5.59	9.71	79.08	5.96	9.78
25	C ₁₈ H ₁₃ ClN ₂ O*0.14CH ₂ Cl ₂	67.91	4.17	8.73	67.88	4.54	8.82
26	C ₂₀ H ₁₉ N ₃ O*0.02CHCl ₃	75.06	5.99	13.11	75.00	6.37	13.28
27	C ₂₁ H ₂₀ N ₂ O ₂	75.88	6.06	8.43	75.64	6.41	8.50
28	C ₂₂ H ₂₂ N ₂ O	79.97	6.71	8.48	79.99	7.01	8.52
29	C ₁₉ H ₁₃ F ₃ N ₂ O	66.67	3.83	8.18	66.48	3.97	8.24
30	C ₁₈ H ₁₂ Cl ₂ N ₂ O *0.15CH ₂ Cl ₂	61.18	3.48	7.86	61.15	3.85	8.00
31	C ₁₈ H ₁₃ ClN ₂ O*0.06CHCl ₃	68.54	4.16	8.84	68.52	4.00	9.01
32	C ₁₉ H ₁₆ N ₂ O ₂ *0.03 CHCl ₃	74.17	5.24	9.09	74.16	5.08	9.21
33	C ₁₉ H ₁₆ N ₂ O	79.14	5.59	9.71	78.74	5.48	9.77
34	C ₁₈ H ₁₃ ClN ₂ O	70.02	4.24	9.07	69.63	4.47	9.09
35	C ₁₈ H ₁₂ Cl ₂ N ₂ O	62.99	3.52	8.16	62.63	3.53	8.18
36	C ₂₀ H ₁₈ N ₂ O ₃	71.84	5.43	8.38	71.48	5.38	8.33
37	C ₁₈ H ₁₅ N ₃ O	74.72	5.23	14.52	74.42	5.69	14.25
38	C ₂₁ H ₂₀ N ₂ O ₂	75.88	6.06	8.43	75.69	6.30	8.25
39	C ₂₀ H ₁₉ N ₃ O*0.10CHCl ₃	73.11	5.83	12.72	73.05	6.03	12.96

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